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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,854	07/17/2003	Chiang J. Li	25627-501	2920

30623 7590 01/17/2006

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EXAMINER	
LEWIS, AMY A	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 01/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/622,854	LI, CHIANG J.	
	Examiner	Art Unit	
	Amy A. Lewis	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) *55-72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 July 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/8/04 & 10/15/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Case & Response to Election/Restriction

Claims 55-72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Applicant's election, without traverse, of Group II (claims 1-54), and the species 3,4-dihydro-4,4-dimethyl-2H-naptho[1,2-b]thiopyran-5,6-dione and E2F1 in the reply filed on 21 November 2005 is acknowledged.

Claims 1-54, as filed 17 July 2003, are presented for examination.

Drawings

The drawings are objected to under 37 CFR 1.83(b) because they are incomplete: Drawings 12 and 13 do not contain axis labels and therefore it is unclear as to what the drawings are demonstrating.

See 37 CFR 1.83(b), which reads as follows:

> When the invention consists of an improvement on an old machine the drawing must when possible exhibit, in one or more views, the improved portion itself, disconnected from the old structure, and also in another view, so much only of the old structure as will suffice to show the connection of the invention therewith.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must

be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

Claims 17, 34, and 51 are objected to because of the following informalities: it appears that the term "minosine" should read ---mimosine---. Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1) Claims 1-54 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-45 and 94-111 of copending Application No. 10/007352 (US Patent Application Publication No. US 2002/0169135 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other because both directed to treating cancer by administering a drug which modulates the G1 and/or S phase of the cell cycle and induces apoptosis, preferably β-lapachone derivatives. Both applications also include methods of treatment by administering a combination of the G1 and/or S phase drug with a drug which modulates the G2/M phase of the cell cycle, with taxanes, microtubule targeting drugs, or topoisomerase inhibitors as the preferred second agent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant needs to file a terminal disclaimer over each of the patents to obviate the rejections. In addition, Applicant is advised to review all pending application for issues of double type patenting. Applicant needs to file a terminal disclaimer over each of the patents to obviate the rejections. In addition, Applicant is advised to review all pending application for issues of double type patenting. The following is a list of known patents and applications with obviousness type double patenting issues:

US Patent Application Nos.:
10/866751 (US Pub. No. 20050097926)
10/887009 (US Pub. No. 20040253216)

10/995565 (No US Pub. No. assigned)
11/068459 (US Pub. No. 20050197406)
11/069637 (US Pub. No. 20050171031)
11/201097 (No US Pub. No. assigned)

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2) Claims 1-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting the growth of cancer cells or tumor growth of prostate cancer (in DLD1 cells), colon cancer (in SW480, HT-29 cells), breast cancer (in MCF-7 cells), pancreatic cancer (in PaCa-2 cells), and lung cancer (in A549 cells), with 3,4-dihydro-4,4-dimethyl-2H-naptho[1,2-b]thiopyran-5,6-dione (the elected species), 3,4-dihydro-2,2-dimethyl-2H-naptho[1,2-b]thiopyran-5,6-dione, 3,4-dihydro-2,2-dimethyl-3-(3-methyl-2-butenyl)-2H-naptho[1,2-b] pyran-5,6-dione, and β-lapachone, does not reasonably provide enablement for preventing or inhibiting the growth of all types of cancer cells or all types of tumor growth *in vivo* with any compound that is a modulator of cell cycle checkpoint activation.

Also, the specification while be enabled for treating human pancreatic cancer cells (in Paca-2 cells) with a combination of β-lapachone and gemcitibine, it is not enabled for combination chemotherapy with any compound that is a modulator of cell cycle checkpoint activation and any chemotherapeutic agent to treat all types of cancer cells or all types of tumor growth.

Further, the specification while being enabled for induction of the transcription factor E2F-2 in colon cancer cells SW480, HT29, and pancreatic cells PANC1 by treatment with 3,4-dihydro-4,4-dimethyl-2H-naptho[1,2-b]thiopyran-5,6-dione (the elected species), 3,4-dihydro-2,2-dimethyl-2H-naptho[1,2-b]thiopyran-5,6-dione, 3,4-dihydro-2,2-dimethyl-3-(3-methyl-2-butenyl)-2H-naptho[1,2-b] pyran-5,6-dione, and β-lapachone, the specification is not enabled for induction of any other transcription factors, including E2F-1 or E2F-3, or induction by treatment with any other compounds other than 3,4-dihydro-4,4-dimethyl-2H-naptho[1,2-b]thiopyran-5,6-dione (the elected species), 3,4-dihydro-2,2-dimethyl-2H-naptho[1,2-b]thiopyran-5,6-dione, 3,4-dihydro-2,2-dimethyl-3-(3-methyl-2-butenyl)-2H-naptho[1,2-b] pyran-5,6-dione, and β-lapachone.

Regarding claim 52 in particular, the specification does not reasonably provide enablement for chemo***prevention*** (emphasis added). The burden of enabling the prevention of a condition such as malignant neoplasia would be much greater than that of enabling the treatment of the condition. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of preventing an apoptosis associated disorder (e.g. cancer) or how a patient could be kept from every being susceptible to this condition. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active agents for preventing apoptosis associated conditions. The term "prevention" is synonymous with the term "curing" and both circumscribe methods of absolute success. Since absolute success is not reasonably possible with most diseases/conditions, especially those having etiologies and pathophysiological manifestations as complex as cancer for instance, the specification, which lacks an objective showing that

apoptosis associated conditions can actually be prevented, is viewed as lacking an adequate written description of the same.

Regarding the limitation "wherein said dosage does not affect non-cancerous cell viability" in instant claims 2, 19, and 36, the specification and examples do not demonstrate this property. Further, the fact that Applicant has demonstrated an IC50 value in normal cell lines (colon and breast) indicates that there is also an LD50 value (lethal dose 50), and therefore the compound will be toxic at a high enough concentration. Thus, the specification is not enabling for not affecting non-cancerous cell viability without a specified dose.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) Nature of the invention.
2) State of the prior art.
3) Relative skill of those in the art.
4) Level of predictability in the art.
5) Amount of direction or guidance provided by the inventor.
6) Presence or absence of working examples.
7) Breadth of the claims.
8) Quantity of experimentation necessary to make or use the invention based on the content of the disclosure.

The instant specification fails to provide guidance that would allow the skilled artisan to

practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth hereinbelow.

1) The nature of the invention.

The claimed invention relates generally to chemotherapy, and specifically to compositions and methods for inhibiting the proliferation of cancer cells and tumor growth without regard to the environment (see instant claim 9) which includes both *in vitro* and *in vivo*.

2) State of the prior art.

While the state of the art is relatively high with regard to the treatment of specific cancer types, the state of the art with regard to treating cancer broadly is underdeveloped. In particular, there is no known anticancer agent that is effective against all cancer cell types. The Cecil reference (Textbook of Medicine, 21st Edition (2000), Goldman & Bennett (Editors), W.B. Saunders Company (Publisher), Chapter 198, pages 1060-1074) clearly shows that for the various known cancer types, there is no one specific chemotherapeutic agent that is effective for all types of cancer (see page Table 198-5 at page 1065; Tables 198-6 and 198-7 at page 1066; Table 198-8 at page 1068; and Table 198-9 at page 1071).

3) Relative skill of those in the art.

The relative skill of those in the art is high, generally that of a PHD/MD with several years of practical experience.

4) Level of predictability in the art.

The cancer treatment art involves a very high level of unpredictability as

demonstrated by the state-of-the-art with regard to the treatment of specific cancers with specific agents and has long been underdeveloped with regard to the treatment of cancers broadly (see discussion in section *2)* above on the state of the prior art). The lack of significant guidance from the present specification or prior art with regard to the actual treatment of all types of cancer cells in a mammal, including a human subject, with the claimed active ingredients/combinations makes practicing the claimed invention unpredictable.

5) Amount of direction or guidance provided by the inventor & 6) Presence or absence of working examples.

The specification at pages 30-37 and Table 1 (on p. 33) teach the specific treatment of prostate cancer (in DLD1 cells), colon cancer (in SW480, HT-29 cells), breast cancer (in MCF-7 cells), pancreatic cancer (in PaCa-2 cells), and lung cancer (in A549 cells), and induction of E2F-2, with 3,4-dihydro-4,4-dimethyl-2H-naptho[1,2-b]thiopyran-5,6-dione (the elected species), 3,4-dihydro-2,2-dimethyl-2H-naptho[1,2-b]thiopyran-5,6-dione, 3,4-dihydro-2,2-dimethyl-3-(3-methyl-2-butenyl)-2H-naptho[1,2-b] pyran-5,6-dione, and β-lapachone. In reference to combination chemotherapy, the specification at pages 36-37 teach the treatment of human pancreatic cancer cells (in Paca-2 cells) with a combination of β-lapachone and gemcitibine.

7) Breadth of claims.

The claims are very broad and inclusive of cancer cells and tumors generally. The breadth of the claims exacerbate the complex nature of the subject matter to which the present claims are directed. The claims are extremely broad due to the vast number

of possible cancer types represented by the terms "cancer" and "apoptosis-associated doscorder" and the vast number of possible combinations of chemotherapeutic agents.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The specification does not enable any person skilled in the art to which it pertains (i.e. chemotherapy and treatment of cancer) to make or use the invention commensurate in scope with the claims. The lack of adequate guidance from the specification or prior art with regard to the actual prevention or treatment of all cancers, or other "apoptosis associated disorder", with 3,4-dihydro-4,4-dimethyl-2H-naptho[1,2-b]thiopyran-5,6-dione (the elected species), 3,4-dihydro-2,2-dimethyl-2H-naptho[1,2-b]thiopyran-5,6-dione, 3,4-dihydro-2,2-dimethyl-3-(3-methyl-2-butenyl)-2H-naptho[1,2-b] pyran-5,6-dione, and β-lapachone fails to rebut the presumption of unpredictability existent in this art. Applicants fail to provide the guidance and information required to ascertain which particular type of cancer the claimed anticancer agent/combination will be effective against without resorting to undue experimentation. Applicant's limited disclosure with respect to β-lapachone in combination with gemcitibine is noted but does not demonstrate treating all cancers or all combinations of 3,4-dihydro-4,4-dimethyl-2H-naptho[1,2-b]thiopyran-5,6-dione (the elected species), 3,4-dihydro-2,2-dimethyl-2H-naptho[1,2-b]thiopyran-5,6-dione, 3,4-dihydro-2,2-dimethyl-3-(3-methyl-2-butenyl)-2H-naptho[1,2-b] pyran-5,6-dione, and β-lapachone with any chemotherapeutic agent.

Absent a reasonable *a priori* expectation of success for using a specific chemotherapeutic agent/combination to treat any particular type of cancer, one skilled in the art would have to extensively test many various tumor types. Since each prospective embodiment, and indeed future embodiments as the art progresses, would have to be empirically tested, and those which initially failed tested further, an undue amount of experimentation would be required to practice the invention as its is claimed in its current scope, because the specification provides inadequate guidance to do otherwise.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3) Claim 52 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "apoptosis associated disorder" in claim 52 is a relative term, which renders the claim indefinite. In particular, "apoptosis associated disorder" does not particularly point out the degree or type of association that a given disorder may have in relation to process of apoptosis and still be considered an "apoptosis associated" as intended by applicants. While Applicants have provided a list of disorders that "may result from a defect in cell cycle checkpoint control and cell death regulation" (see p. 5 of the specification), Applicants have failed to provide any

specific definition for this term in the present specification. Lacking a clear meaning of the term "apoptosis associated disorder", the skilled artisan would not be reasonably apprised of the metes and bounds of the subject matter for which Applicant seeks patent protection.

Words and phrases in the claims must be given their "plain meaning" as understood by one having ordinary skill in the art unless defined by Applicant in the specification with "reasonable clarity, deliberateness and precision" (MPEP 2111.01). Thus, the identity of those disorders that are included or excluded by the term "apoptosis associated disorder" are open to subjective interpretation and such is inconsistent with the requirements of 35 U.S.C. §112, second paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4) Claims 1-54 are rejected under 35 U.S.C. 102(b) as being anticipated by Pardee et al. (US Patent No. 6,875,745 B2).

Pardee et al. teach a method for treating a mammalian tumor by administering a G1 and/or S phase drug, preferably the topoisomerase I inhibitor β-lapachone or a derivative or analog of β-lapachone, in combination with a G2/M phase drug, preferably taxane or a derivative or analog of taxane (see: abstract; col. 2, lines 45-65). The reference states that "molecular changes underlying cell cycle delay at multiple checkpoints, for example G1 and/or S phase and

G2/M phase, can for example result in synergistic induction of apoptosis in malignant cells" (col. 5, lines 21-26). The combination reduces tumor burden load and/or regresses tumor growth, with the specific cancers to be treated including breast, ovarian, prostate, lung, colon, and melanoma (see: col. 7, lines 59-65; Figs 6 and 7; Examples 1-4; Table 2 at col. 17).

The reference teaches that the compounds can be administered by any means known in the art, including parenteral, intravenous, oral, and topical, thus meeting the limitations of instant claims 11-14 (see col. 7 line 66 – col. 8, line 3). The reference also describes pharmaceutically acceptable dosage formulations (col. 12, lines 31-51).

The reference teaches administration of the cell checkpoint activation drug in combination with a chemotherapeutic agent. The preferred G2/M phase checkpoint targeting drugs to be used in combination with the G1/S phase β-lapachone derivatives include microtubule targeting drugs (for example, taxol, docetaxel, vincristine, vinblastin, nocodazole, epothilones, navelbine, and methotrexate) and topoisomerase poisons (for example, teniposide, etoposide, adriamycin, camptothecin, daunorubicin, dactinomycin, mitoxantrine, amsacrine, epirubicin, and idarubicin). See: col.4, line 5 – col. 7, line 62; Table 1.

The reference teaches the β-lapachone derivative 3,4-dihydro-2,2-dimethyl-3-(3-methyl-2-butenyl)-2H-naptho[1,2-b] pyran-5,6-dione, of instant claim 9: Formula V where R7 is an aleknyl (see col. 11).

Regarding the specific limitation (in instant claims 2, 19, and 36), "not toxic to non cancerous cells" is interpreted as "toxic to cancerous cells," therefore treatment of cancer with the claimed composition/combination meets this limitation.

Regarding the specific limitation wherein the cell checkpoint modulator elevates the level of a member of the E2F family of transcription factors, including E2F-1, E2F-2, and E2F-3 (of instant claims 18 and 35), this functional language as well as an inherent property of a drug which would induce apoptosis via modlulating the S phase of the cell cycle, such as the β-lapachone derivatives of the Pardee et al. reference. In the instant case, Wang A, et al. ("Cancer chemotherapy by deoxynucleotide depletion and E2F-1 elevation," September 1, 2005 *Cancer Res.* 65(17): 7809-7814) demonstrates that "the lethality of commonly used anticancer drugs, eg.g methotrexate...are due, at least in part, to an increase of the E2F-1 mediated apoptotic cascade." And that the "E2F family acts to provide control of S phase transcribing genes required for deoxynecleoside triphosphate and DNA synthesis" (see abstract). Therefore, the property of elevating levels of E2F transcription factors is an inherent property of the β-lapachone derivatives and β-lapachone derivatives in combination with other chemotherapeutic drugs, as taught by Pardee et al., thus meeting the limitations of instant claims 18-51.

Also see M.P.E.P. § 2124 regarding the date of reference used to demonstrate an inherent property, which states:

> In certain circumstances, **references cited to show a universal fact need not be available as prior art before applicant's filing date**. Such facts include the characteristics and properties of a material or a scientific truism. Some specific examples in which later publications showing factual evidence can be cited include situations where the facts shown in the reference are evidence "that, as of an application 's filing date, undue experimentation would have been required, or that a parameter absent from the claims was or was not critical, or that a statement in the specification was inaccurate,

or that the invention was inoperative or lacked utility, or that a claim was indefinite, or that characteristics of prior art products were known. However, it is impermissible to use a later factual reference to determine whether the application is enabled or described as required under 35 U.S.C. 112, first paragraph. **References which do not qualify as prior art because they postdate the claimed invention may be relied upon** to show the level of ordinary skill in the art at or around the time the invention was made." See M.P.E.P. § 2124 for relevant citations.

5) Claims 1, 2, 4-13, 15-17 and 52-54 are rejected under 35 U.S.C. 102(b) as being anticipated by Jaing Z and Reddy D (US Patent Application Pub. No. US 2004/00717755 A1, with a priority date of 21 July 2001).

Jaing and Reddy teach β-lapachone and derivatives for the treatment of cancer (abstract). The reference demonstrates growth inhibition in ovary, breast, melanoma, colon, pancreas, lung, and prostate cancer cell lines (see: Table 9 at [0139] and Fig. 4). The reference also describes several *in vivo* mouse xenograft tumor models (see: [0142-0152]; Figs 14-17). The pharmaceutical β-lapachone derivative compositions may be administered with a second anticancer agent, especially paclitaxel (see: abstract; paragraph [0047]). The reference also describes pharmaceutical preparations for parenteral and/or oral administration ([0049]).

The Jaing and Reddy reference also teaches several specific β-lapachone derivatives, including 3,4-dihydro-2,2-dimethyl-3-(3-methyl-2-butenyl)-2H-naptho[1,2-b] pyran-5,6-dione (see Fig. 12, bottom row, middle compound).

Pertinent Art:

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

- Pardee et al. (US Patent No. 6,245,807 B1) teaches the β-lapachone derivative 3,4-dihydro-2,2-dimethyl-3-(3-methyl-2-butenyl)-2H-naptho[1,2-b] pyran-5,6-dione, of instant claims 9, 26, and 43, for the treatment of prostate cancer: the compound of Formula I where R can be a substituted or unsubstituted alkenyl (see: abstract; claim 1).
- Arqule, Inc./ Jaing Z, et al. (WO 2004/045557 A2, with a priority date of 18 November 2002). Jaing et al. teach the lapachone derivatives 3,4-dihydro-4,4-dimethyl-2H-naptho[1,2-b]thiopyran-5,6-dione (the elected species) as well as 3,4-dihydro-2,2-dimethyl-2H-naptho[1,2-b]thiopyran-5,6-dione, both of instant claims 9, 26, and 43, for the treatment of cell proliferative disorders, including cancer. See: abstract; Fig. 1 compounds 1 and 6.
- Dyson N. ("The regulation of E2F by pRB-family proteins," 1998 *Genes & Development* 12: 2245-2262) reviews the function of E2F transcription factors. In particular, the reference summarizes the role E2F-1 plays in cell cycle progression (i.e. S-phase entry), cell proliferation, and apoptosis.

Conclusion

Claims 1-54 are rejected. No claims are allowed.

The elected species 3,4-dihydro-4,4-dimethyl-2H-naptho[1,2-b]thiopyran-5,6-dione is free of the prior art.

Contact Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy A. Lewis whose telephone number is (571) 272-2765. The examiner can normally be reached on Monday-Friday, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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